UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

JOHN HANCOCK LIFE INSURANCE COMPANY, JOHN HANCOCK VARIABLE LIFE INSURANCE COMPANY, and MANULIFE INSURANCE COMPANY (f/k/a INVESTORS PARTNER INSURANCE COMPANY), Plaintiffs, vs. ABBOTT LABORATORIES, Defendant.	Civil Action No. 05-11150-DPW Hon. Judge Douglas P. Woodlock

ABBOTT'S OBJECTIONS TO THE AFFIDAVIT OF DR. BARRY I. GOLD

1. Abbott objects to the following paragraphs of the Affidavit of Dr. Barry I. Gold, filed January 28, 2007, on the grounds that they are untimely under Federal Rule of Civil Procedure 26(a)(2)(B) because they constitute new opinions that were not disclosed in Dr. Gold's initial "Summary of Anticipated Expert Testimony of Dr. Barry I. Gold," ("Gold I") served on October 13, 2006, or in his "Updated Summary of Anticipated Testimony of Dr. Barry I. Gold," ("Gold II") dated November 30, 2007: 19-22, 36-38, 51, 71, 72, 76-80, 82, 84, 87-89, and 93. A true and correct copy of Gold I is attached hereto as Exhibit A and a true and correct copy of Gold II is attached hereto as Exhibit B. Abbott objects on the same grounds to paragraph 26 of Dr. Gold's affidavit, with the exception of the phrase "ABT-773 failed to meet its target profile", and to the first sentence of paragraph 35, in which Dr. Gold also states new

opinions not previously disclosed. The Court should exclude the above-referenced paragraphs of Dr. Gold's affidavit, as well as any testimony concerning these subjects.

The Court set the deadline for service of expert reports in this matter for October 13, 2006. According to the report Dr. Gold submitted on that date, he was "asked . . .to provide the court with an expert tutorial on the research and development of new pharmaceutical compounds, particularly among large pharmaceutical companies." Gold I, p. 1. Although his report stated that he "may also be called upon to comment on particular activities or events in Abbott's research and development of certain compounds encompassed by the Research Funding Agreement entered into by John Hancock and Abbott in March 2001," in fact Dr. Gold did not do so in his report. To the contrary, the report mentions Abbott only in two places. First, at page 3, Dr. Gold includes "Abbott" as an example of a company that would be included in his definition of "Big Pharma". Second, at page 8, Dr. Gold references a clinical study protocol for an ABT-518 Phase I study for the purpose of illustrating Dr. Gold's general point that "clinical trial protocols usually also define precisely what is being measured". At no point in Gold I does Dr. Gold otherwise mention Abbott or purport to apply his general observations regarding "the research and development of new pharmaceutical compounds, particularly among large pharmaceutical companies" to Abbott. Similarly, Dr. Gold makes no reference in Gold I to any aspect of the research and development of ABT-594 or ABT-773. The reference to ABT-518 set forth above is his only mention of that compound.

Pursuant to the Court's Order filed on October 25, 2007, and entered on October 29, 2007, the parties were permitted to file "Updated, Final Versions of Their Expert Reports" no later than December 1, 2007. Hancock submitted Gold II in response to this Order. Gold II is virtually identical to Gold I, with the following exceptions. First, at page 5 of Gold II, Dr. Gold

added two paragraphs discussing the FDA's Pediatric Rule. He did not mention Abbott in these additional paragraphs. Second, at page 6 of Gold II Dr. Gold added the phrase "For new INDs" as the prefatory phrase to a sentence that was in Gold I regarding the submission of proposed protocols to the FDA by a pharmaceutical company. Third, at page 7, Dr. Gold modified one sentence in a paragraph of general comments about clinical monitors and physician investigators. In Gold II, Dr. Gold added nothing to his previous very limited references to Abbott and to ABT-518. As in Gold I, Dr. Gold said nothing whatsoever in Gold II about ABT-594 or ABT-773.

In striking contrast, Dr. Gold's trial affidavit is replete with opinions specifically about Abbott and about ABT-518, ABT-594, and ABT-773, as well as with other new opinions and comments. For example, at paragraphs 35-38, Dr. Gold for the first time opines that Abbott's development of a backup compound for ABT-594 was an indication of Abbott's supposed concerns about the "viability and prospects for ABT-594." No such opinion was disclosed in either Gold I or Gold II. Similarly, at paragraphs 50-51 and at paragraphs 76-84, Dr. Gold for the first time offers opinions on Abbott's conduct of and supposed reactions to clinical trials and results for ABT-518, ABT-594 and ABT-773. None of these opinions were disclosed in Gold I or Gold II.

Federal Rules of Civil Procedure 26(a)(2)(B) and 37(c)(1) forbid the kind of surprise tactics exemplified by the previously undisclosed opinions in the Gold affidavit. Under Rule 26, the expert's report must "contain a complete statement of all opinions to be expressed and the basis and reasons therefore." Fed. R. Civ. P. 26(a)(2)(B) And the Court properly exercises its "gatekeeper" function in striking expert testimony that goes beyond that disclosed in the expert's report. *See, e.g., See Boardman v. National Med. Enters.*, 106 F.3d 840, 843 (8th Cir. 1997) (affirming exclusion of expert opinions not disclosed in report, but raised for first time during

deposition). Moreover, Hancock's violation of Rule 26 is particularly egregious here because on October 25, 2007, the Court gave the parties the opportunity to update their expert reports, yet Dr. Gold failed to include any of his new opinions in that updated report. At the Pretrial Conference on October 25, 2007, the Court made clear that the updated expert report was to contain all of the expert's opinions in a refined form, "so that, as the Court stated, the parties would know "what his last -- or her last and best offer is about testimony." Transcript, October 25, 2007 Pretrial Conference, p. 49. True and correct copies of the relevant pages of the transcript of the October 25, 2007 Pretrial conference are attached hereto as Exhibit C. Indeed, even had Dr. Gold included his new opinions referenced above in Gold II, they would have been untimely, since, as the Court stated at the Pretrial Conference, the updated reports were not to include new opinions. *Id.* at 50 ("we'll use the December 1 date for the submission of the final expert reports which will be simply refinements and not expansions of the opinions that they rendered within the discovery period").

In the Gold affidavit, Hancock intends for Dr. Gold to offer entirely new opinions even though Hancock failed to disclose these opinions in either of Dr. Gold's expert reports. Hancock cannot meet its burden under Rule 37(c)(1) of showing that its violation of Rule 26(a) was either justified or harmless. The sanction of preclusion of the opinions of Dr. Gold in the paragraphs of his affidavit referenced above is therefore mandatory. *See Silong v. United States*, No. CV F 06-0474 LJO DLB, 2007 WL 2712100 (E.D. Cal. Sept. 14, 2007) (entering "mandatory" exclusion order for failure to comply strictly with Rule 26 requirements).[1]

[1] For both factual and legal reasons, Hancock cannot argue that Dr. Gold's deposition testimony cures its failure to provide an adequate report. First, Dr. Gold did not, in fact, testify at his deposition to the previously undisclosed opinions and their bases referenced above. Second, and more importantly, the law prohibits Hancock from remedying shortcomings in their experts' reports by relying on their experts' deposition testimony. *See, e.g., Silong, 2007 WL 2712100 at *4-5; Ferriso v. Conway Organization*, 1995 WL 580197 at *3 (S.D.N.Y. Oct. 3, 1995) (rejecting argument that deposition testimony served as

2. Abbott objects to paragraphs 21, 35, 38, 71, 77, 78, 80 and 89 of Dr. Gold's affidavit on the ground that Dr. Gold's opinions in these paragraphs as to Abbott's supposed state of mind or motives, including without limitation what Abbott and/or its employees allegedly "believed", "suspected", "doubted," "concluded," or had "concerns" about is improper, incompetent, and is inadmissible under Rule 702 of the Federal Rules of Evidence. Abbott also objects on the same grounds to Dr. Gold's opinion at paragraph 26 that Abbott terminated development of ABT-773 "because, among other things, ABT-773 failed to meet its target profile." (emphasis added). Abbott further objects to Dr. Gold's opinion at paragraph 51 that "FDA representatives expressed concern regarding the safety profile" of ABT-773. (emphasis added).

Rule 702 permits witnesses qualified as experts to offer opinion testimony only if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case. Fed. R. Evid. 702. Under Rule 702, the trial judge "must ensure that any and all scientific testimony or evidence admitted is not only relevant, but reliable." *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 589 (1993); *see also Kumho Tire Co., Ltd. v. Carmichael*, 526 U.S. 137, 149 (1999) (extending *Daubert*'s requirements to all expert testimony). The Court should exclude an expert report that does not meet the *Daubert* standards even in a bench trial because the purpose of *Daubert* is to "assist the trier of fact to understand or determine a fact in issue" and to ensure that the "expert testimony is relevant and helpful." *See Williams v. Poulos*, 11 F.3d 271, 282 (1st Cir. 1993) (motion in limine excluding expert report

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"implicit amendment" to written expert disclosure required by Rule 26). Of course, permitting deposition testimony to supplant expert reports would eliminate any incentive for parties to comply with Rule 26(a). *See generally Ortiz v. Sociedad Espanola*, 248 F.3d 29, 35 (1st Cir. 2001) (explaining that preclusion sanction in Rule 37(c)(1) is intended to "uphold and facilitate" compliance with Rule 26(a)).

properly granted in bench trial); *Seaboard Lumber Co. v. U.S.*, 308 F.3d 1283, 1302 (Fed. Cir. 2002) ("While these concerns are of lesser import in a bench trial, where no screening of the factfinder can take place, the *Daubert* standards of relevance and reliability for scientific evidence must nevertheless be met.").

An expert may not be called to testify as to a party's state of mind -- what that party was thinking or knew or intended. *See, e.g., CMI-Trading, Inc. v. Quantum Air, Inc.*, 98 F.3d 887, 890 (6th Cir. 1996) ("The intent of the parties is an issue within the competence of the jury and expert opinion testimony will not assist the jury, within the meaning of Federal Rule of Evidence 702, in determining the factual issue of intent."). Such testimony is no more appropriate as applied to the state of mind of a corporation or its employees. *See DePaepe v. General Motors Corp.*, 141 F.3d 715, 720 (7th Cir. 1998) (holding that trial court erred by allowing expert to testify as to why General Motors had reduced the amount of padding in its automobile sun visors because expert "lacked any scientific basis for an opinion about the motives of GM's designers"); *In re Rezulin Products Liability Litig.*, No. 00 Civ. 2843, 2004 U.S. Dist. LEXIS 3104, * 21 (S.D.N.Y. Feb. 27, 2004) ("[T]he opinions of these witnesses on the intent, motives or states of mind of corporations, regulatory agencies and others have no basis in any relevant body of knowledge or expertise.").

Moreover, even if expert testimony about the state of mind of Abbott or its employees were otherwise admissible, Dr. Gold has no expertise in such matters. Dr. Gold is not an expert on human psychology or corporate decision-making. In his affidavit, Dr. Gold highlights his qualifications in pharmacology, biochemistry and clinical research. Neither his education nor his experience qualify him to render an expert opinion regarding the mental states of other individuals during the relevant period. *See Sassafras Enters. v. Roshco, Inc.*, 915 F. Supp. 1, 8

(N.D. Ill. 1996) (finding nothing in a business expert's experience that suggests his qualifications as a "mind reader"). Absent any conceivable expert basis for his conclusions about what Abbott allegedly "believed", "suspected", doubted", "concluded", or had "concerns" about, Dr. Gold is simply acting as an advocate for Hancock's version of the facts. The cases make clear such advocacy cannot be introduced into evidence through "expert" testimony. *See Rezulin*, 2004 U.S. Dist. LEXIS 3104, at * 21-22 ("[P]laintiffs' experts propose improperly to assume the role of advocates for the plaintiffs' case by arguing as to the intent or motives underlying the conduct of [defendant] or others, a transgression that has resulted in the exclusion of 'expert' testimony as to the 'real motive' behind certain business transactions.") (citing cases).

An expert witness "must be qualified in the specific subject for which his testimony is offered." *Whiting v. Boston Edison Co.*, 891 F. Supp. 12, 24 (D. Mass. 1995) Stripped of its expert aura, Dr. Gold's testimony about the state of mind of Abbott (and the FDA) is merely his own lay opinion based on some (but by no means all) of the same evidence presented to the Court. Because Dr. Gold's expertise does not qualify him to opine on the mental state of others, there is nothing in the sections of his affidavit referenced above amounting to expert or scientific knowledge that is "helpful" to the fact finder under Rule 702. The Court should therefore exclude the above-referenced paragraphs of Dr. Gold's affidavit concerning the state of mind or motives of Abbott, Abbott's personnel, or the FDA, as well as any testimony concerning these subjects, as unqualified speculation under Rule 702.

3. Abbott objects to paragraphs 59 and 60 of Dr. Gold's affidavit on the ground that he is not qualified to testify about the subject matter of those two paragraphs. As discussed in section 2 above, an expert witness "must be qualified in the specific subject for which his testimony is offered." *Whiting v. Boston Edison Co.*, 891 F. Supp. at 24. The specific subject

matter of paragraphs 59 and 60 is the role of statisticians, what the "power" of a study supposedly means to statisticians, and what degree of power is "considered statistically valid". Dr. Gold has no expertise in statistics and no experience as a statistician. At his deposition, he acknowledged that he did not have a degree in statistics, had taken only one course in the subject, and had never worked as a statistician in the pharmaceutical industry. Gold Deposition, pp. 30-31. Dr. Gold's testimony about statistical questions is therefore incompetent and inadmissible. Accordingly, the Court should exclude paragraphs 59 and 60 of Dr. Gold's affidavit, as well as any testimony concerning these subjects.

4. Abbott objects to paragraphs 26, 36, 37, 51, 71, 72, 76, 77, 78, 82, 83, 84, 89 and 93 of Dr. Gold's affidavit on the ground that the opinions expressed in these paragraphs are nothing more than Dr. Gold's own lay opinion based on the same evidence presented to the Court. There is nothing in these paragraphs, which purport to set forth Dr. Gold's conclusions about what Abbott did or did not do or think about various issues, that is "helpful" to the fact finder under Rule 702. Dr. Gold's opinions in these paragraphs amount to nothing more than improper advocacy for Hancock's version of the facts. *See Rezulin*, 2004 U.S. Dist. LEXIS 3104, at * 21-22. An expert cannot simply tell the fact finder, in this case the Court, what to think about the evidence and the facts. *See Montgomery v. Aetna Casualty & Surety Co.*, 898 F.2d 1537, 1541 (11th Cir. 1990) ("An expert may not . . .merely tell the [fact finder] what result to reach."). The Court should therefore exclude these paragraphs of Dr. Gold's affidavit, as well as any testimony concerning these subjects.

5. With respect to the exhibits attached to Dr. Gold's affidavit, Abbott incorporates by reference the objections stated in Abbott's Objections to Hancock's Proposed Trial Exhibits, filed January 28, 2008, as revised.[2]

ABBOTT LABORATORIES

By its attorneys

/s/ Gregory D. Phillips
Gregory D. Phillips

Michael S. D'Orsi
Peter E. Gelhaar (BBO #188310)
Michael S. D'Orsi (BBO #566960)
DONNELLY, CONROY & GELHAAR LLP
1 Beacon St., 33rd Floor
Boston, Massachusetts 02108
(617) 720-2880

and

Jeffrey I. Weinberger (Admitted Pro Hac Vice)
Gregory D. Phillips (Admitted Pro Hac Vice)
Eric J. Lorenzini (Admitted Pro Hac Vice)
Ozge Guzelsu (Admitted Pro Hac Vice)
MUNGER, TOLLES & OLSON LLP
355 South Grand Avenue, 35th Floor
Los Angeles, CA 90071
(213) 683-9100

Dated: February 28, 2008

[2] As noted in Abbott's opposition to Hancock's Motion to Overrule Authenticity and Various Hearsay Objections, Abbott plans to file a revised and narrower set of objections to Hancock's trial exhibits on February 29, 2008. Until such time, Abbott reserves its right to object to exhibits on the grounds stated in its Objections to Hancock's Proposed Trial Exhibits, filed January 28, 2008.

CERTIFICATE OF SERVICE

I hereby certify that this document(s) filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF) and paper copies will be sent to those indicated as non registered participants on February 28, 2008.

Date: February 28, 2008.

/s/ Eric J. Lorenzini

Exhibit A

Barry I. Gold, Ph.D.
217 Lane Gate Road
Cold Spring, NY 10516
Tele: 845-265-2210

Summary of Anticipated Expert Testimony of Dr. Barry I. Gold

The following is a summary of the anticipated expert testimony of Dr. Barry I. Gold in connection with the action entitled John Hancock Life Insurance Company, John Hancock Variable Life Insurance Company, and Manulife Insurance Company (f/k/a Investors Partner Insurance Company) v. Abbott Laboratories, U.S.D.C. (Mass.) Civil Action No. 05-11150-DPW. Dr. Gold has been asked by Choate, Hall & Stewart LLP, on behalf of John Hancock Life Insurance Company, John Hancock Variable Life Insurance Company, and Manulife Insurance Company, (collectively "John Hancock"), to provide the court with an expert tutorial on the research and development of new pharmaceutical compounds, particularly among large pharmaceutical companies. Dr. Gold also may be called upon to comment on particular activities or events in Abbott's research and development of certain compounds encompassed by the Research Funding Agreement entered into by John Hancock and Abbott in March 2001.

Dr. Gold is a consultant to the pharmaceutical industry who received a B.S. in zoology from the University of Cincinnati and a Ph.D. in pharmacology from Boston University. He won a 3-year postdoctoral fellowship to Yale University School of Medicine, after which he was Assistant Professor of Pharmacology at the Uniformed Services University School of Medicine for six years. Dr. Gold thereafter was employed in the pharmaceutical industry as Group Leader of Biochemistry at Anaquest. He moved into pharmaceutical development after Anaquest as Associate Director of

Clinical Research at Roberts Pharmaceuticals, then as Director of Project Management for Central Nervous System and Biologicals at Wyeth, and later as Director of Project Management at Knoll Pharmaceutical. Dr. Gold was employed by Abbott briefly after Abbott acquired Knoll Pharmaceutical in or about 2001. As an independent consultant, Dr. Gold provides advice and assistance concerning drug development to pharmaceutical companies. A copy of Dr. Gold's current professional C.V. is appended to this summary as Exhibit 1.

Dr. Gold will testify based upon his own experience, upon information and materials in the public domain (including, but not limited to, information from the United States Food and Drug Administration's ("FDA") website and reports from Public Citizen and Tufts University), and upon testimony and materials obtained in discovery in this action. During his tutorial, Dr. Gold may make reference to specific evidence contained in documents or witness testimony. A list of key documents that Dr. Gold has relied upon to date for purposes of preparing his anticipated testimony is appended to this summary as Exhibit 2.

Dr. Gold is being compensated on an hourly basis for the work that he performs in this matter. His billing rate is $250 per hour plus expenses, and his compensation is unrelated to the outcome of this litigation. Dr. Gold has not testified as an expert at trial or by deposition within the preceding four years.

Dr. Gold's work in this matter is not yet complete. He expects that the substance of his planned tutorial and his opinions may change to prior to trial based upon his ongoing analysis and/or events that may occur in the course of this litigation, including the production of additional documents and new deposition or trial testimony.

He reserves the right to change or modify his opinions and anticipated testimony in light of such analysis or event. Dr. Gold also expects to utilize a PowerPoint or similar graphic presentation during the course of his tutorial, a copy of which will be provided to Abbott reasonably in advance of trial.

Dr. Gold is expected to testify about drug research and development ("R&D") in the pharmaceutical industry, with emphasis on R&D within what is commonly referred to as "Big Pharma." For purposes of his testimony, Dr. Gold will define Big Pharma as those pharmaceutical companies with an annual R&D budget that typically exceeds $1 billion, including, but not limited to, Pfizer, Johnson and Johnson, Wyeth, GlaxoSmithKline, Bristol-Meyers Squibb and Abbott.

Dr. Gold is expected to provide an overview of the R&D process that will include a discussion of both the preclinical and the clinical phases of development. His discussion of the preclinical phase will include testimony regarding how new pharmaceutical compounds or "molecules" typically are discovered or identified. He will discuss how and why compounds are synthesized by chemists or extracted from natural products, or licensed from one company to another or from independent research centers, including universities. He will address how a target drug profile is developed, how compounds are screened to meet that profile, how specific development candidates typically are selected, and the role of backup compounds in the development process. He will discuss the importance of product differentiation in the marketplace, and its role in developing target product profiles. He will supply explanations and examples of drug screening, preclinical testing, and selecting compounds for clinical development. He will address the use of *in vitro* experimental models, as well as

preclinical measures of cardiac safety, toxicology, genotoxicity, fetotoxicity, and other important drug characteristics and properties. He will discuss the types and significance of both positive and negative preclinical data and results.

Dr. Gold is expected to testify concerning the clinical research and testing process, including the various phases of clinical research. It is anticipated that he will define the three primary phases of clinical research, consistent with FDA practice, as follows:

Phase I includes the initial introduction of an investigational new drug into humans. These studies usually are conducted in healthy volunteer subjects and are designed to determine the metabolic and pharmacological actions of the drug in humans, the side effects associated with increasing doses and, if possible, to gain early evidence of effectiveness. Phase I studies also evaluate drug metabolism, structure-activity relationships, and the mechanism of action in humans. The total number of subjects included in Phase I studies is generally in the range of twenty to eighty.

Phase II includes the early controlled clinical studies conducted to obtain some preliminary data on the effectiveness of the drug for a particular indication or indications in patients with the disease or condition. This phase of testing also helps determine the common short-term side effects and risks associated with the drug. Phase II studies usually involve several hundred people. Phase "IIa" and Phase "IIb" are not official FDA nomenclature. Phase IIa studies commonly are defined as tests on a limited number of patients to obtain proof of principle and to test for tolerance and safety. Phase IIb studies commonly are defined as tests to verify the effects seen during Phase IIa studies and to determine the optimal dosages. Many companies follow the

FDA's standard nomenclature and do not divide their Phase II studies into "IIa" and "IIb" categories.

Phase III studies typically are designed to gather the additional information about effectiveness and safety that is needed to statistically evaluate the overall benefit-risk relationship of the compound. Phase III studies also are intended to provide an adequate basis for extrapolating the results to the general population and transmitting that information in the physician labeling. Phase III studies usually include several hundred to several thousand people. Two Phase III clinical trials usually are required by FDA as pivotal proof of efficacy.

Dr. Gold is expected to explain that, at the end of the clinical development program, the sponsoring company may file a New Drug Application ("NDA") with the FDA, which, if and when approved, becomes a license to market, ship and sell the new compound in the United States.

Dr. Gold is expected to discuss average duration and cost for each clinical phase in the pharmaceutical industry, and will address the standard regulatory filings that are required by FDA at each stage under federal law. He will describe the Investigational New Drug Application ("IND") process, and the various types of IND submissions and their contents. He is expected to discuss the requirements for an Institutional Review Board ("IRB"), a Statement of Investigator (Form 1572), the Pre-IND meeting with FDA and typical timetables for initiating clinical trials. He will discuss Case Report Forms (CRFs), the concept and application of trial "blinding," and data flow between clinical investigators and the sponsoring companies. He also will explain the NDA

process, the Prescription Drug User Fee Act ("PDUFA"), and the typical communications with and from FDA.

Dr. Gold is expected to testify concerning the typical planning, structure and operation of clinical trials. He will discuss how clinical trials are designed and organized, how they generate data, how the data is collected and analyzed, and the types and significance of both positive and negative clinical data and results. Clinical trials usually are designed and managed by a clinical monitor who is typically an employee of the sponsoring drug company. Occasionally, the monitoring role is contracted to a clinical research organization ("CRO"), which functions as a contractor/partner of the pharmaceutical company. The trial is designed in a document known as a "protocol" or "clinical protocol." The flow of each protocol typically is similar. The responsible committees within the drug company approve it internally, then it is sent to the FDA as part of the IND that the company files for that particular compound. If the company receives no objection from the FDA within thirty days of submitting its proposed protocol, the company may initiate the study.

Dr. Gold further is expected to testify that, at or about the time that the company submits the protocol to the FDA, the clinical monitor arranges with physician investigators (who are not employees of the sponsoring pharmaceutical company) to execute the trial. Most clinical trials are too large for one investigator, so they typically are spread out among many investigators and different institutions. This is commonly referred to in the pharmaceutical industry as a "multi-center" trial. Some investigators typically are medical school faculty, and some are in private or group practice. The investigators are not paid by the company for their work, but they do

receive grants to cover their expense of treating the patient and maintaining the necessary records. The amount usually is negotiated in advance. Medical school faculty members typically are paid by their school and it is the school administration that negotiates the grant with the pharmaceutical company. Invariably, medical schools keep a portion of the grant as overhead for administering the grant. The amount of overhead varies among schools and can be as large as one hundred percent, thereby effectively doubling the cost of the trial.

Dr. Gold further is expected to testify that a proposed clinical trial protocol usually also is presented to an Institutional Review Board ("IRB") for review. If the trial is to be run at a medical school, then the IRB typically is attached to the medical school, but it is not necessarily composed of employees of the medical school. The IRB is charged with evaluating the protocol with regard to guarding patient's safety, ensuring that the Informed Consent required of each patient is understandable and truly informs the patient, and ensuring that the protocol is consistent with medical and local ethics. If the trial is run by a private-practice physician or in a private group, the IRB is local and not attached to any institution. Physician-investigators may not initiate a protocol without their applicable IRB's approval.

Dr. Gold is expected to describe the principal design elements of a clinical study protocol. All protocols are written to define the study variables. That is, each investigator agrees to do the same tests on each patient, to evaluate each patient in the same manner, and to measure the same data. Any observations made outside the defined study variables usually are considered irrelevant to the study results, unless they are adverse events. The protocol defines how many patients need to be enrolled

by making certain assumptions about statistical variability in the data. One or more statisticians usually are involved in the development of the protocol and the statistician's duties typically include estimating very closely how many patients must be enrolled in order to detect a statistically significant difference between placebo and the test drug, or between different doses of the test drug. To statisticians, the "power" of a study refers to the statistical test they have chosen and the probability that the test will fail to detect a true difference between two groups. Calculating the power of the trial requires the statistician first to specify the size of the effect that he or she wishes to detect. The greater the effect size (*i.e.*, the difference in effect between two treatment groups), the greater the power of the study. Although there are no formal standards for power, most researchers who assess the power of their studies use 0.80 as a standard for adequacy, and pharmaceutical companies frequently will require that a trial "reach 80% power" in order to be considered statistically valid.

Dr. Gold is expected to testify that clinical trial protocols usually also define precisely what is being measured. For example, Abbott's ABT-518 compound was studied in a protocol entitled "A Phase I Escalating Multiple Dose Study of Matrix Metalloproteinase Inhibitor (ABT-518) in Patients with Advanced Cancer." The primary objectives of the trial were: (1) to establish a safety profile of ABT-518 given orally once a day; (2) to determine the maximum tolerated dose (MTD) of the ABT-518 when administered orally for 27 days. Three secondary objectives were defined also: (1) to determine the pharmacokinetics of ABT-518 in patients; (2) to determine a dose level for Phase II studies; and (3) to describe any preliminary evidence of anti-tumor activity. The success or failure of a particular trial turns not only on the results

obtained, but on its ability, in the first instance, to provide the data that is sought. A trial that is aborted or terminated prior to completion such that the data do not have the desired statistical significance generally is not regarded in the pharmaceutical industry as a "successful" trial.

Dr. Gold further is expected to testify that Big Pharma companies usually manage drug development using project teams, defined as a multidisciplinary staff of employees who are assigned temporarily to report to a project team leader. The team's assignment is to manage the overall development of a particular compound or group of related compounds, from discovery through registration. At most companies, project team members are drawn from preclinical research, clinical research, toxicology, marketing, pharmaceutical sciences and regulatory affairs. Team structure is fluid and can vary from company to company. Most Big Pharma companies' project teams, however, report to a research committee that usually is chaired by the head of clinical research.

Dr. Gold further is expected to testify that drug development project teams usually report directly to senior R&D management. In addition to directing the development process, the teams typically are charged with responsibility to keep senior management apprised of the development status, cost versus budget issues, and emerging issues that could affect the status of the compound under development, including changes that could extend the registration past the expected target date, or communications to or from FDA. Dr. Gold is expected to offer examples of circumstances or events that could cause a pharmaceutical company to elect to prematurely terminate a clinical trial. In this context, Dr. Gold is expected to discuss

the nature and identification of adverse events and premature terminations, how they typically are reported both within large pharmaceutical companies and to the FDA, and what role and significance they typically have in the development decision-making process.

Dr. Gold is expected to describe how R&D management typically is kept apprised of clinical trial progress and why the circulation of such information to management is important. Drug development is expensive, with Phase III trials frequently costing in millions of dollars each. Big Pharma companies manage the development process to minimize risk, maximize successful registration, keep their portfolios up to date with new medications and provide a return on investment for their shareholders. They do so by managing their portfolio of development compounds and deleting or discontinuing compounds when their risk of failure significantly rises, by accelerating investment in compounds when their probability of success increases, and by managing the total number of compounds in development so their annual R&D budgets do not become overextended.

Dr. Gold is expected to provide examples of significant development issues and events that typically are expected to be presented or communicated to senior R&D management without delay. These include, but are not limited to, a permanent or temporary hold on a clinical trial, untoward or unexpected adverse events or premature patient terminations during a clinical trial, the early termination of a clinical trial due to adverse events or a substantial number of premature patient terminations, budgetary overruns and manufacturing problems. Additionally, team members usually are required to promptly report "bad news" to their line managers and their project team

leaders, and project team leaders usually are required to report significant project news immediately to R&D senior management. Failure to do so can result in job loss.

Dr. Gold is expected to testify that senior R&D management usually places considerable emphasis on timely reporting because of the amount of money at stake in the development process. For example, Pfizer reports on its website that it budgets $7.4 billion a year for pharmaceutical R&D, thereby claiming the industry's largest R&D expenditure. At that rate, Pfizer spends approximately $20.2 million a day on R&D activities. While Pfizer does not publicize the number of compounds in its portfolio, it would be reasonable to assume that Pfizer has roughly 20 compounds in various stages of clinical development and that it is spending, on average, about $1 million per day on each compound in development. If Pfizer's senior R&D management was not apprised immediately of significant adverse events or other trouble in a clinical trial such that the trial went on one day more than prudent management would permit, that delay could cost the company $1 million. No pharmaceutical company would sanction its senior management wasting such large amounts of money on a misinformed or ill-timed decision. That is why senior R&D management typically places such extreme emphasis on timely reporting from its project teams.

Dr. Gold further is expected to testify that development project team members usually also are charged with studying the relevant scientific literature for new technology, news from other companies, including those that have research programs in the same areas and those that do not, and news from medical schools or government research agencies. Occasionally, news from other companies or from government

research agencies can have a direct bearing on a pharmaceutical company's clinical research plans, and project team members are expected to communicate such news to senior R&D management promptly.

Dr. Gold is expected to provide additional testimony regarding the operation of clinical trials. Clinical trials of pharmaceutical compounds are governed by, among other things, applicable FDA rules and requirements and by medical ethics, especially as interpreted by the relevant institutional review boards ("IRBs"). There are many reasons to halt a trial, an activity known within the pharmaceutical industry as a "clinical hold." First and foremost is the ethical consideration of "do no harm." If an investigator, an IRB or a company's clinical monitor determines that patient safety is compromised, it is their responsibility to halt the trial. While all drugs can cause adverse reactions or events (also referred to as "side-effects"), some adverse events are innocuous, manageable, expected and/or dose-related. If, on the other hand, an adverse event is not expected or dose-related, or it is not within the drug candidate's target profile, the company's clinical monitor will discuss it with his or her management while the trial is underway. An adverse event that threatens patient safety, that results in death, or that is so uncomfortable that patient enrollment is slowed or too many patients drop out of the trial (also referred to a "premature terminations") frequently will lead senior R&D management officials to halt the trial. Similarly, if a serious adverse event is reported to the company and, as required by law, also reported to FDA, then the FDA can choose to place the trial on clinical hold.

Dr. Gold is expected to testify that most Phase II and Phase III clinical trials are "blinded" or "double-blinded." A double-blinded trial is one in which the investigating

physician does not know whether he or she is administering an investigational drug, as opposed to a placebo or active control, to any particular patient, and the patient does not know what he or she is receiving. Since the data collected during a clinical trial usually are a mixture of machine measurements, such the patient's blood pressure, and the physician's and/or the patient's subjective observations, such as a ranking of pain or some other reaction on a scale from one to ten, there is considerable room in the trial process for what is referred to as "observational bias." Blinding the trial provides a means of guarding against observational bias.

Dr. Gold further is expected to testify that, although blinded clinical trials typically remain blinded until after the study has been concluded, a great deal of data still are provided by the investigators to the company's clinical monitor and the company while the trial is underway. For example, all demographic data are reported to the company. Such data would include a patient's age, gender, weight, height, other illnesses and diagnosis. In addition, adverse events are reported to the clinical monitor, sometimes daily and sometimes "online." A high number of adverse events during a clinical trial can be a signal that the trial results are likely to be negative, especially if the protocol specifies an intent-to-treat analysis, and can have a devastating effect on the long term commercial prospects for compound being studied. Furthermore, if too many patients suffer adverse reactions or events, drop out of the study prematurely because of adverse events, or die as a result of the study drug, the clinical monitor or the company may halt the trial and report the decision to the project team leader and R&D management. There is a double motivation to report such problems in a timely

manner, the first being the ethical responsibility to "do no harm," and the second being the fiduciary responsibility held by all team members.

Dr. Gold further is expected to testify that, while a clinical trial is underway, the clinical monitor at the company typically stays in close contact with the study investigators. Each investigational site usually is monitored by an employee of the pharmaceutical company, sometimes called a "clinical research associate" or "CRA," or by an outside monitor who is retained to perform the duties of the CRA. The CRA's job is to ensure that each investigator maintains a case report form ("CRF") for each patient, that the CRF is kept up-to-date, and that all data entered into the CRF is in accord with the primary documents in the patient's records. The CRF data will be transferred to the pharmaceutical company only after the CRFs have been inspected by the CRA. Some Big Pharma companies have begun using electronic CRFs or electronic data collection. Such companies have access to the demographic data and the adverse events in real time, that is, almost instantaneously.

Dr. Gold is expected to describe the patient enrollment process that typically is used in clinical trials. Enrollment can affect the speed and duration of a clinical trial for a variety of reasons. For example, some protocols are written to restrict or exclude what are referred to as "comorbidities," that is, patients who have more than one disease or condition. In other instances, rumors can pass among study patients or prospective study patients that whatever compound they are taking makes them sick or simply does not work. The net result in both instances can be slow enrollment. Furthermore, a series of adverse events in a trial can slow enrollment because the investigators begin to appreciate that the trial is not going well, which can dampen the

investigators' enthusiasm for enrolling new patients. Sometimes enrollment is so slow that the clinical monitor at the pharmaceutical company must intervene either by opening more research sites, by offering a financial incentive to the investigators, or by hiring a patient recruitment company to assist in to the enrollment process. These patient recruitment companies typically advertise widely, sometimes on television, in newspapers and on the Internet, to find suitable patients.

Dr. Gold is expected to testify that a clinical trial typically ends when the last patient receives his or her last blinded dose and the patient has been followed for the time specified in the protocol. Then the sponsoring company will monitor the investigator one last time and "bring the data in house," which means the Case Report Forms are brought back to the sponsoring company. Most companies scan the CRFs into an electronic record and enter all the trial data into an electronic database. The data then are reviewed and any inconsistencies are reconciled. Only then will the patient data be unblinded, that is, the specific drug and dose information will be assigned to each patient record. The patient data then will be sorted into groups by dose and drug, and one or more statistical tests will be applied. Typically, an early data report will be presented to the head of the clinical department within a few days after the data have been unblinded.

Dr. Gold further is expected to testify that before and during a compound's clinical development, senior R&D management defines a variety of "Go/No Go" decisions that will determine the compound's fate. Some of these decisions represent regulatory hurdles, some examine the development compound's agreement or disagreement with the target product profile, and some react to data coming in from

clinical trials. For example, examination of a compound's deviation from its target profile is a decision point that is repeated throughout the development cycle. For example, Abbott's ABT-773 diverged from its target profile by not achieving once daily dosing in "3 of 4 respiratory indications," did not have a "side-effect profile any better or worse" than a standard medication in the same class, and seemed to fall short of "achieving a resistance claim." There also was concern that "safety issues remain to be better defined ... the potential for QT prolongation, and the incidence and severity of liver enzyme abnormalities." *See* ABBT-220661 and 220662.

Dr. Gold further is expected to testify that when a compound is or is about to be terminated for any reason during clinical development, many Big Pharma companies begin to develop a "backup" or "replacement" compound. The hope and expectation in such circumstances is that the small difference in the molecular structure between the terminated compound and the backup will be sufficient to overcome the difficulty that caused the first compound's failure. Pharmacology is mechanism-based and it is the compound's mechanism of action that drives its appeal, not necessarily its structure. Thus, one compound with less desirable characteristics may be terminated in favor a slightly different compound from the same family or class that demonstrates more desirable characteristics, or at least less unpleasant characteristics.

Dr. Gold further is expected to testify that pharmaceutical companies have an active ongoing trade of compounds with other pharmaceutical companies. They buy compounds, trade their own compounds for others, license compounds or the underlying technology. They do business with universities, with government and private labs and small biotechnology companies. They try to supplement their own

research labs, to gain access to new technology and to rationalize their development portfolios. This latter activity can take many forms. Companies will fill gaps in their portfolios by in-licensing compounds. They will also divest compounds if they have too many new compounds in a single therapeutic area. Similarly, they will in-license compounds to enter a new therapeutic area. They out-license compounds that have run into difficulty in clinical trials or compounds whose mechanism is not understood even after investing millions of dollars. They find niche companies, such as Biovail, whose business it is to profit by reformulating difficult molecules, or those whose only business is to develop Phase II or Phase III drugs and then license them again to a company that will market it. The Medicines Company is an example of latter business model. It is customary in the pharmaceutical industry that all data surrounding a compound is disclosed to a potential licensor under a confidentiality agreement, especially the status and results of all clinical trials.

EXHIBIT 1

Barry I. Gold, Ph.D.

217 Lane Gate Road
Cold Spring, NY 10516

barry.gold@att.net
845-265-2210 home office
973-615-4089 cell

Extensive pharmaceutical industry experience in:

- Due diligence analysis, both licensing and M&A
- Alliance development, management and strategy
- Portfolio management, developing drugs and therapeutic areas
- Drug discovery, development portfolio management

PROFESSIONAL EXPERIENCE

Consultant to the Pharmaceutical Industry — ***2004 – present***

Contract consultant for three Washington-area consulting companies in project design and budgeting, sourcing, drug candidate review and product defense. Expert witness testimony.

Great Harvest Bread Co® — ***2002 – 2004***
Franchise Owner/Manager — ***Westfield, NJ***

Purchased franchise, negotiated lease, managed store construction
Equipped store, trained staff, ran production, training & sales
Forecast budgets, developed P&L statements
Negotiated sublease & liquidated the business

Knoll Pharmaceutical Co. — ***1998 – 2001***
Director, Project Management — ***Mt. Olive, NJ, Nottingham, UK Ludwigshafen, Germany***

Drafted department mission and goals
Managed cancer and pain developmental portfolios internationally
Filed U.S. and European registrations for Dilaudid XR
Forecast budget; tracked expenses, reported to Board of Directors
Managed Dilaudid project transition to Abbott

Wyeth-Ayerst Research (now Wyeth) — ***1994 – 1998***
Director, Project Management, CNS & Biologicals — ***Radnor, PA Paris, FR***

Managed Central Nervous System & vaccine developmental portfolios internationally
Managed alliances with Alza, Servier, Interneuron, Scios and Asta-Medica
Registered Ef(f)exor XR and Sonata in U.S. and Europe
Managed transition of CNS portfolio after Lederle acquisition
Chaired CNS Therapeutic Area Council, developed strategic direction

The Genesis Group ***1993 – 1994***
Consultant ***Montclair, NJ***

Developed pharmaceutical industry intelligence & reported in their newsletter
Privately developed business plans, raised capital & attempted leveraged buyout of a small pharmaceutical company. Consulted on project design to startup companies

Roberts Pharmaceutical Corp. (now Shire) ***1992 – 1993***
Associate Director, Clinical Research ***Eatontown, NJ***

Managed clinical trials, out-license efforts and alliance development
Introduced project- and team-management into development

Export Management for Science ***1990 – 1992***
Consultant ***Summit, NJ***

Developed alliances between U.S. & offshore technology companies
Built an E-commerce business before the Internet

Anaquest, Division of the BOC Group ***1984 – 1989***
Group Leader, Biochemistry ***New Providence, NJ***

Recruited from academics to build and manage a biochemical pharmacology laboratory
Reviewed licensing opportunities and chaired anew technology surveillance committee

Uniformed Services University of the Health Sciences ***1978 – 1984***
Assistant Professor ***Bethesda, MD***

Managed medical research laboratory and taught second-year medical students
Consulted to pharmaceutical companies

EDUCATION

Bachelor of Science, Zoology
University of Cincinnati, Cincinnati, OH

Doctor of Philosophy, Pharmacology
Boston University, Boston, MA
Received the Sandoz Award for contribution to health care

Postdoctoral Fellow, Pharmacology and Psychiatry
Yale University, New Haven, CT
Received U.S. Government National Research Service Awards for postdoctoral study

OTHER PROFESSIONAL ACTIVITY

Adjunct faculty, Jersey City State College, Jersey City, NJ (1992 – 1997)
Director, National Health Association, Summit, NJ Chapter (1993)
Feature article writer, published in Woman's Day and others
Expert witness for counsel
Authored book on the history of aspirin (pending)

HONORS

Listed in: Who's Who in Frontier Science and Technology;
American Men and Women of Science
Member of Governor Whitman's (NJ) Council on Drug Abuse Prevention
Member of Governor's Speaker's Bureau
Member of American Society for Pharmacology and Experimental Therapeutics

EXHIBIT 2

Barry I. Gold, Ph.D.
217 Lane Gate Road
Cold Spring, NY 10516

Exhibit 2

Documents Referenced

ABT-594

Type	Accession # begin	Accession # end	Date
Patient Quest Proposal	ABBT240985		26-Sep-00
IND Safety Report	ABBT236700		28-Oct-00
Project Review	ABBT0019102	ABBT0019136	17-Nov-00
email	ABBT326427		30-Nov-00
email	ABBT233539		14-Dec-00
Project Review ppt	ABBT0025450	ABBT0025474	2-Feb-01
Success Prob. Summary	ABBT0012431		6-Feb-01
email	ABBT335154		4-Mar-01
Decision Analysis	ABBT298380	ABBT298382	5-Mar-01
Seminar Invitation	ABBT0022006	ABBT0022008	12-Mar-01
Decision Analysis	ABBT0022081	ABBT0022092	21-Aug-01
email	ABBT245659		9-Oct-01
email	ABBT245657		10-Oct-01

ABT-518

Patient Quest quote	ABBT240985		26-Sep-00
IND Safety Report	ABBT236700		28-Oct-00
Project Review	ABBT0019102	ABBT0019136	17-Nov-00
email	ABBT326427		30-Nov-00
email	ABBT233539		14-Dec-00
Project Review	ABBT0025450	ABBT0025474	2-Feb-01
Summary of success	ABBT0012431		6-Feb-01
email	ABBT335154		4-Mar=01
Pain strategy dec. anal	ABBT298380	ABBT298382	5-Mar-01
Seminar announcement	ABBT0022006	ABBT00222008	12-Mar-01
Core Team Mtg sched.	ABBT329250		13-Mar-01
Decision analysis	ABBT0022081	ABBT0022092	21-Apr-01
email	ABBT246253		28-Sep-01
email	ABBT245659		9-Oct-01
email	ABBT245657		10-Oct-01

ABT-773

Decision support group	ABBT111378	ABBT111386	8-Mar-00
Decision support group	ABBT111398	ABBT111399	8-Mar-00
Update	ABBT205047	ABBT205064	12-Feb-01
Memo, Sun to Bukofzerr	ABBT204959	ABBT205046	22-Feb-01
Memo, Leiden to list	ABBT209487	ABBT209488	10-Dec-01
Memo, Sun to Leonard et al.	ABBT231340	ABBT231342	3-Jan-02
Interoffice memo	ABBT220661	ABBT220662	
Desccriptive memo	ABBT245921	ABBT245926	1-Feb

General Reference

Public Citizen website	http://www.citizen.org/hrg//drugs/index.cfm

Barry I. Gold, Ph.D.
217 Lane Gate Road
Cold Spring, NY 10516

Exhibit 2

Tufts Center for the Study of Drug I	http://csdd.tufts.edu/	
Intent-to-Treat Analysis	ACR/ARHP Ann. Mtg*	27-Oct-03

*Amer. College of Rheumatology & Assoc. of Rheumatology Health Professionals

Exhibit B

Barry I. Gold, Ph.D.
217 Lane Gate Road
Cold Spring, NY 10516
Tele: 845-265-2210

Updated Summary of Anticipated Expert Testimony of Dr. Barry I. Gold

The following is an updated summary of the anticipated expert testimony of Dr. Barry I. Gold in connection with the action entitled John Hancock Life Insurance Company, John Hancock Variable Life Insurance Company, and Manulife Insurance Company (f/k/a Investors Partner Insurance Company) v. Abbott Laboratories, U.S.D.C. (Mass.) Civil Action No. 05-11150-DPW. Dr. Gold has been asked by Choate, Hall & Stewart LLP, on behalf of John Hancock Life Insurance Company, John Hancock Variable Life Insurance Company, and Manulife Insurance Company, (collectively "John Hancock"), to provide the court with an expert tutorial on the research and development of new pharmaceutical compounds, particularly among large pharmaceutical companies. Dr. Gold also may be called upon to comment on particular activities or events in Abbott's research and development of certain compounds encompassed by the Research Funding Agreement entered into by John Hancock and Abbott in March 2001.

Dr. Gold is a consultant to the pharmaceutical industry who received a B.S. in zoology from the University of Cincinnati and a Ph.D. in pharmacology from Boston University. He won a 3-year postdoctoral fellowship to Yale University School of Medicine, after which he was Assistant Professor of Pharmacology at the Uniformed Services University School of Medicine for six years. Dr. Gold thereafter was employed in the pharmaceutical industry as Group Leader of Biochemistry at Anaquest. He moved into pharmaceutical development after Anaquest as Associate Director of Clinical

Research at Roberts Pharmaceuticals, then as Director of Project Management for Central Nervous System and Biologicals at Wyeth, and later as Director of Project Management at Knoll Pharmaceutical. Dr. Gold was employed by Abbott briefly after Abbott acquired Knoll Pharmaceutical in or about 2001. As an independent consultant, Dr. Gold provides advice and assistance concerning drug development to pharmaceutical companies. A copy of Dr. Gold's current professional C.V. is appended to this summary as Exhibit 1.

Dr. Gold will testify based upon his own experience, upon information and materials in the public domain (including, but not limited to, information from the United States Food and Drug Administration's ("FDA") website and reports from Public Citizen and Tufts University), and upon testimony and materials obtained in discovery in this action. During his tutorial, Dr. Gold may make reference to specific evidence contained in documents or witness testimony. A list of key documents that Dr. Gold has relied upon to date for purposes of preparing his anticipated testimony is appended to this summary as Exhibit 2.

Dr. Gold is being compensated on an hourly basis for the work that he performs in this matter. His billing rate is $250 per hour plus expenses, and his compensation is unrelated to the outcome of this litigation. Dr. Gold has not testified as an expert at trial or by deposition within the preceding four years.

Dr. Gold expects that the substance of his planned tutorial and his opinions may change prior to trial based upon his ongoing analysis and/or events that may occur in the course of this litigation, including the production of additional documents and new deposition or trial testimony. He reserves the right to change or modify his opinions and anticipated testimony in light of such analysis or event. Dr. Gold also expects to utilize a

PowerPoint or similar graphic presentation during the course of his tutorial, a copy of which will be provided to Abbott reasonably in advance of trial.

Dr. Gold is expected to testify about drug research and development ("R&D") in the pharmaceutical industry, with emphasis on R&D within what is commonly referred to as "Big Pharma." For purposes of his testimony, Dr. Gold will define Big Pharma as those pharmaceutical companies with an annual R&D budget that typically exceeds $1 billion, including, but not limited to, Pfizer, Johnson and Johnson, Wyeth, GlaxoSmithKline, Bristol-Meyers Squibb and Abbott.

Dr. Gold is expected to provide an overview of the R&D process that will include a discussion of both the preclinical and the clinical phases of development. His discussion of the preclinical phase will include testimony regarding how new pharmaceutical compounds or "molecules" typically are discovered or identified. He will discuss how and why compounds are synthesized by chemists or extracted from natural products, or licensed from one company to another or from independent research centers, including universities. He will address how a target drug profile is developed, how compounds are screened to meet that profile, how specific development candidates typically are selected, and the role of backup compounds in the development process. He will discuss the importance of product differentiation in the marketplace, and its role in developing target product profiles. He will supply explanations and examples of drug screening, preclinical testing, and selecting compounds for clinical development. He will address the use of *in vitro* experimental models, as well as preclinical measures of cardiac safety, toxicology, genotoxicity, fetotoxicity, and other important drug characteristics and

properties. He will discuss the types and significance of both positive and negative preclinical data and results.

Dr. Gold is expected to testify concerning the clinical research and testing process, including the various phases of clinical research. It is anticipated that he will define the three primary phases of clinical research, consistent with FDA practice, as follows:

Phase I includes the initial introduction of an investigational new drug into humans. These studies usually are conducted in healthy volunteer subjects and are designed to determine the metabolic and pharmacological actions of the drug in humans, the side effects associated with increasing doses and, if possible, to gain early evidence of effectiveness. Phase I studies also evaluate drug metabolism, structure-activity relationships, and the mechanism of action in humans. The total number of subjects included in Phase I studies is generally in the range of twenty to eighty.

Phase II includes the early controlled clinical studies conducted to obtain some preliminary data on the effectiveness of the drug for a particular indication or indications in patients with the target disease or condition. This phase of testing also helps determine the common short-term side effects and risks associated with the drug. Phase II studies usually involve several hundred people. Phase "IIa" and Phase "IIb" are not official FDA nomenclature. Phase IIa studies commonly are defined as tests on a limited number of patients to obtain proof of principle and to test for tolerance and safety. Phase IIb studies commonly are defined as tests to verify the effects seen during Phase IIa studies and to determine the optimal dosages. Many companies follow the FDA's standard nomenclature and do not divide their Phase II studies into "IIa" and "IIb" categories.

Phase III studies typically are designed to gather the additional information about effectiveness and safety that is needed to statistically evaluate the overall benefit-risk relationship of the compound. Phase III studies also are intended to provide an adequate basis for extrapolating the results to the general population and transmitting that information in the physician labeling. Phase III studies usually include several hundred to several thousand people. Two Phase III clinical trials usually are required by FDA as pivotal proof of efficacy.

Dr. Gold is expected to explain that, at the end of the clinical development program, the sponsoring company may file a New Drug Application ("NDA") with the FDA, which, if and when approved, becomes a license to market, ship and sell the new compound in the United States.

Dr. Gold is also expected to explain that in 1994, FDA issued a regulation requiring that sponsoring companies review existing data to determine if those data could support adding information to the drug's labeling about pediatric use. Sponsoring manufacturers were encouraged, but not required, to submit a supplemental NDA (sNDA) seeking such a labeling change.

Dr. Gold is expected to explain further than in December 1998, FDA issued its Pediatric Rule, first proposed in 1977 (the "1998 Rule"). The 1998 Rule required all drugs and biologicals that were not yet approved to be studied in pediatric patients. FDA defined pediatric patients as those between 2 and 18 years old. The 1998 Rule also authorized FDA to require pediatric studies as a condition of approval of drugs and biologicals under some circumstances.

Dr. Gold is expected to discuss average duration and cost for each clinical phase in the pharmaceutical industry, and will address the standard regulatory filings that are required by FDA at each stage under federal law. He will describe the Investigational New Drug Application ("IND") process, and the various types of IND submissions and their contents. He is expected to discuss the requirements for an Institutional Review Board ("IRB"), a Statement of Investigator (Form 1572), the Pre-IND meeting with FDA and typical timetables for initiating clinical trials. He will discuss Case Report Forms (CRFs), the concept and application of trial "blinding," and data flow between clinical investigators and the sponsoring companies. He also will explain the NDA process, the Prescription Drug User Fee Act ("PDUFA"), and the typical communications with and from FDA.

Dr. Gold is expected to testify concerning the typical planning, structure and operation of clinical trials. He will discuss how clinical trials are designed and organized, how they generate data, how the data is collected and analyzed, and the types and significance of both positive and negative clinical data and results. Clinical trials usually are designed and managed by a clinical monitor who is typically an employee of the sponsoring drug company. Occasionally, the monitoring role is contracted to a clinical research organization ("CRO"), which functions as a contractor/partner of the pharmaceutical company. The trial is designed in a document known as a "protocol" or "clinical protocol." The flow of each protocol typically is similar. The responsible committees within the drug company approve it internally, then it is sent to the FDA as part of the IND that the company files for that particular compound. For new INDs, if

the company receives no objection from the FDA within thirty days of submitting its proposed protocols, the company may initiate human studies.

Dr. Gold further is expected to testify that, at or about the time that the company submits the protocol to the FDA, the clinical monitor arranges with physician investigators (who are not employees of the sponsoring pharmaceutical company) to execute the trial. Most clinical trials are too large for one investigator, so they typically are spread out among many investigators and different institutions. This is commonly referred to in the pharmaceutical industry as a "multi-center" trial. Some investigators typically are medical school faculty, and some are in private or group practice. Investigators are paid by companies for their work, usually in the form of grants to cover their expense of treating the patient and maintaining the necessary records. There is some profitability built in and grant amounts are usually is negotiated in advance. Medical school faculty members typically are paid by their school and it is the school administration that negotiates the grant with the pharmaceutical company. Invariably, medical schools keep a portion of the grant as overhead for administering the grant. The amount of overhead varies among schools and can be as large as one hundred percent, thereby effectively doubling the cost of the trial.

Dr. Gold further is expected to testify that a proposed clinical trial protocol usually also is presented to an Institutional Review Board ("IRB") for review. If the trial is to be run at a medical school, then the IRB typically is attached to the medical school, but it is not necessarily composed of employees of the medical school. The IRB is charged with evaluating the protocol with regard to guarding patient's safety, ensuring that the Informed Consent required of each patient is understandable and truly informs

the patient, and ensuring that the protocol is consistent with medical and local ethics. If the trial is run by a private-practice physician or in a private group, the IRB is local and not attached to any institution. Physician-investigators may not initiate a protocol without their applicable IRB's approval.

Dr. Gold is expected to describe the principal design elements of a clinical study protocol. All protocols are written to define the study variables. That is, each investigator agrees to do the same tests on each patient, to evaluate each patient in the same manner, and to measure the same data. Any observations made outside the defined study variables usually are considered irrelevant to the study results, unless they are adverse events. The protocol defines how many patients need to be enrolled by making certain assumptions about statistical variability in the data. One or more statisticians usually are involved in the development of the protocol and the statistician's duties typically include estimating very closely how many patients must be enrolled in order to detect a statistically significant difference between placebo and the test drug, or between different doses of the test drug. To statisticians, the "power" of a study refers to the statistical test they have chosen and the probability that the test will fail to detect a true difference between two groups. Calculating the power of the trial requires the statistician first to specify the size of the effect that he or she wishes to detect. The greater the effect size (*i.e.*, the difference in effect between two treatment groups), the greater the power of the study. Although there are no formal standards for power, most researchers who assess the power of their studies use 0.80 as a standard for adequacy, and pharmaceutical companies frequently will require that a trial "reach 80% power" in order to be considered statistically valid.

Dr. Gold is expected to testify that clinical trial protocols usually also define precisely what is being measured. For example, Abbott's ABT-518 compound was studied in a protocol entitled "A Phase I Escalating Multiple Dose Study of Matrix Metalloproteinase Inhibitor (ABT-518) in Patients with Advanced Cancer." The primary objectives of the trial were: (1) to establish a safety profile of ABT-518 given orally once a day; (2) to determine the maximum tolerated dose (MTD) of the ABT-518 when administered orally for 27 days. Three secondary objectives were defined also: (1) to determine the pharmacokinetics of ABT-518 in patients; (2) to determine a dose level for Phase II studies; and (3) to describe any preliminary evidence of anti-tumor activity. The success or failure of a particular trial turns not only on the results obtained, but also on its ability, in the first instance, to provide the data that is sought. A trial that is aborted or terminated prior to completion such that the data do not have the desired statistical significance generally is not regarded in the pharmaceutical industry as a "successful" trial.

Dr. Gold further is expected to testify that Big Pharma companies usually manage drug development using project teams, defined as a multidisciplinary staff of employees who are assigned temporarily to report to a project team leader. The team's assignment is to manage the overall development of a particular compound or group of related compounds, from discovery through registration. At most companies, project team members are drawn from preclinical research, clinical research, toxicology, marketing, pharmaceutical sciences and regulatory affairs. Team structure is fluid and can vary from company to company. Most Big Pharma companies' project teams, however, report to a research committee that usually is chaired by the head of clinical research.

Dr. Gold further is expected to testify that drug development project teams usually report directly to senior R&D management. In addition to directing the development process, the teams typically are charged with responsibility to keep senior management apprised of the development status, cost versus budget issues, and emerging issues that could affect the status of the compound under development, including changes that could extend the registration past the expected target date, or communications to or from FDA. Dr. Gold is expected to offer examples of circumstances or events that could cause a pharmaceutical company to elect to prematurely terminate a clinical trial. In this context, Dr. Gold is expected to discuss the nature and identification of adverse events and premature terminations, how they typically are reported both within large pharmaceutical companies and to the FDA, and what role and significance they typically have in the development decision-making process.

Dr. Gold is expected to describe how R&D management typically is kept apprised of clinical trial progress and why the circulation of such information to management is important. Drug development is expensive, with Phase III trials frequently costing in millions of dollars each. Big Pharma companies manage the development process to minimize risk, maximize successful registration, keep their portfolios up to date with new medications and provide a return on investment for their shareholders. They do so by managing their portfolio of development compounds and deleting or discontinuing compounds when their risk of failure significantly rises, by accelerating investment in compounds when their probability of success increases, and by managing the total number of compounds in development so their annual R&D budgets do not become overextended.

Dr. Gold is expected to provide examples of significant development issues and events that typically are expected to be presented or communicated to senior R&D management without delay. These include, but are not limited to, a permanent or temporary hold on a clinical trial, untoward or unexpected adverse events or premature patient terminations during a clinical trial, the early termination of a clinical trial due to adverse events or a substantial number of premature patient terminations, budgetary overruns and manufacturing problems. Additionally, team members usually are required to promptly report "bad news" to their line managers and their project team leaders, and project team leaders usually are required to report significant project news immediately to R&D senior management. Failure to do so can result in job loss.

Dr. Gold is expected to testify that senior R&D management usually places considerable emphasis on timely reporting because of the amount of money at stake in the development process. For example, Pfizer reports on its website that it budgets $7.4 billion a year for pharmaceutical R&D, thereby claiming the industry's largest R&D expenditure. At that rate, Pfizer spends approximately $20.2 million a day on R&D activities. While Pfizer does not publicize the number of compounds in its portfolio, it would be reasonable to assume that Pfizer has roughly 20 compounds in various stages of clinical development and that it is spending, on average, about $1 million per day on each compound in development. If Pfizer's senior R&D management was not apprised immediately of significant adverse events or other trouble in a clinical trial such that the trial went on one day more than prudent management would permit, that delay could cost the company $1 million. No pharmaceutical company would sanction its senior management wasting such large amounts of money on a misinformed or ill-timed

decision. That is why senior R&D management typically places such extreme emphasis on timely reporting from its project teams.

Dr. Gold further is expected to testify that development project team members usually also are charged with studying the relevant scientific literature for new technology, news from other companies, including those that have research programs in the same areas and those that do not, and news from medical schools or government research agencies. Occasionally, news from other companies or from government research agencies can have a direct bearing on a pharmaceutical company's clinical research plans, and project team members are expected to communicate such news to senior R&D management promptly.

Dr. Gold is expected to provide additional testimony regarding the operation of clinical trials. Clinical trials of pharmaceutical compounds are governed by, among other things, applicable FDA rules and requirements and by medical ethics, especially as interpreted by the relevant institutional review boards ("IRBs"). There are many reasons to halt a trial, an activity known within the pharmaceutical industry as a "clinical hold." First and foremost is the ethical consideration of "do no harm." If an investigator, an IRB or a company's clinical monitor determines that patient safety is compromised, it is their responsibility to halt the trial. While all drugs can cause adverse reactions or events (also referred to as "side-effects"), some adverse events are innocuous, manageable, expected and/or dose-related. If, on the other hand, an adverse event is not expected or dose-related, or it is not within the drug candidate's target profile, the company's clinical monitor will discuss it with his or her management while the trial is underway. An adverse event that threatens patient safety, that results in death, or that is so

uncomfortable that patient enrollment is slowed or too many patients drop out of the trial (also referred to a "premature terminations") frequently will lead senior R&D management officials to halt the trial. Similarly, if a serious adverse event is reported to the company and, as required by law, also reported to FDA, then the FDA can choose to place the trial on clinical hold.

Dr. Gold is expected to testify that most Phase II and Phase III clinical trials are "blinded" or "double-blinded." A double-blinded trial is one in which the investigating physician does not know whether he or she is administering an investigational drug, as opposed to a placebo or active control, to any particular patient, and the patient does not know what he or she is receiving. Since the data collected during a clinical trial usually are a mixture of machine measurements, such the patient's blood pressure, and the physician's and/or the patient's subjective observations, such as a ranking of pain or some other reaction on a scale from one to ten, there is considerable room in the trial process for what is referred to as "observational bias." Blinding the trial provides a means of guarding against observational bias.

Dr. Gold further is expected to testify that, although blinded clinical trials typically remain blinded until after the study has been concluded, a great deal of data still are provided by the investigators to the company's clinical monitor and the company while the trial is underway. For example, all demographic data are reported to the company. Such data would include a patient's age, gender, weight, height, other illnesses and diagnosis. In addition, adverse events are reported to the clinical monitor, sometimes daily and sometimes "online." A high number of adverse events during a clinical trial can be a signal that the trial results are likely to be negative, especially if the protocol

specifies an intent-to-treat analysis, and can have a devastating effect on the long term commercial prospects for compound being studied. Furthermore, if too many patients suffer adverse reactions or events, drop out of the study prematurely because of adverse events, or die as a result of the study drug, the clinical monitor or the company may halt the trial and report the decision to the project team leader and R&D management. There is a double motivation to report such problems in a timely manner, the first being the ethical responsibility to "do no harm," and the second being the fiduciary responsibility held by all team members.

Dr. Gold further is expected to testify that, while a clinical trial is underway, the clinical monitor at the company typically stays in close contact with the study investigators. Each investigational site usually is monitored by an employee of the pharmaceutical company, sometimes called a "clinical research associate" or "CRA," or by an outside monitor who is retained to perform the duties of the CRA. The CRA's job is to ensure that each investigator maintains a case report form ("CRF") for each patient, that the CRF is kept up-to-date, and that all data entered into the CRF is in accord with the primary documents in the patient's records. The CRF data will be transferred to the pharmaceutical company only after the CRFs have been inspected by the CRA. Some Big Pharma companies have begun using electronic CRFs or electronic data collection. Such companies have access to the demographic data and the adverse events in real time, that is, almost instantaneously.

Dr. Gold is expected to describe the patient enrollment process that typically is used in clinical trials. Enrollment can affect the speed and duration of a clinical trial for a variety of reasons. For example, some protocols are written to restrict or exclude what

are referred to as "comorbidities," that is, patients who have more than one disease or condition. In other instances, rumors can pass among study patients or prospective study patients that whatever compound they are taking makes them sick or simply does not work. The net result in both instances can be slow enrollment. Furthermore, a series of adverse events in a trial can slow enrollment because the investigators begin to appreciate that the trial is not going well, which can dampen the investigators' enthusiasm for enrolling new patients. Sometimes enrollment is so slow that the clinical monitor at the pharmaceutical company must intervene either by opening more research sites, by offering a financial incentive to the investigators, or by hiring a patient recruitment company to assist in to the enrollment process. These patient recruitment companies typically advertise widely, sometimes on television, in newspapers and on the Internet, to find suitable patients.

Dr. Gold is expected to testify that a clinical trial typically ends when the last patient receives his or her last blinded dose and the patient has been followed for the time specified in the protocol. Then the sponsoring company will monitor the investigator one last time and "bring the data in house," which means the Case Report Forms are brought back to the sponsoring company. Most companies scan the CRFs into an electronic record and enter all the trial data into an electronic database. The data then are reviewed and any inconsistencies are reconciled. Only then will the patient data be unblinded, that is, the specific drug and dose information will be assigned to each patient record. The patient data then will be sorted into groups by dose and drug, and one or more statistical tests will be applied. Typically, an early data report will be presented to the head of the clinical department within a few days after the data have been unblinded.

Dr. Gold further is expected to testify that before and during a compound's clinical development, senior R&D management defines a variety of "Go/No Go" decisions that will determine the compound's fate. Some of these decisions represent regulatory hurdles, some examine the development compound's agreement or disagreement with the target product profile, and some react to data coming in from clinical trials. For example, examination of a compound's deviation from its target profile is a decision point that is repeated throughout the development cycle. For example, Abbott's ABT-773 diverged from its target profile by not achieving once daily dosing in "3 of 4 respiratory indications," did not have a "side-effect profile any better or worse" than a standard medication in the same class, and seemed to fall short of "achieving a resistance claim." There also was concern that "safety issues remain to be better defined … the potential for QT prolongation, and the incidence and severity of liver enzyme abnormalities." *See* ABBT-220661 and 220662.

Dr. Gold further is expected to testify that when a compound is or is about to be terminated for any reason during clinical development, many Big Pharma companies begin to develop a "backup" or "replacement" compound. The hope and expectation in such circumstances is that the small difference in the molecular structure between the terminated compound and the backup will be sufficient to overcome the difficulty that caused the first compound's failure. Pharmacology is mechanism-based and it is the compound's mechanism of action that drives its appeal, not necessarily its structure. Thus, one compound with less desirable characteristics may be terminated in favor a slightly different compound from the same family or class that demonstrates more desirable characteristics, or at least less unpleasant characteristics.

Dr. Gold further is expected to testify that pharmaceutical companies have an active ongoing trade of compounds with other pharmaceutical companies. They buy compounds, trade their own compounds for others, license compounds or the underlying technology. They do business with universities, with government and private labs and small biotechnology companies. They try to supplement their own research labs, to gain access to new technology and to rationalize their development portfolios. This latter activity can take many forms. Companies will fill gaps in their portfolios by in-licensing compounds. They will also divest compounds if they have too many new compounds in a single therapeutic area. Similarly, they will in-license compounds to enter a new therapeutic area. They out-license compounds that have run into difficulty in clinical trials or compounds whose mechanism is not understood even after investing millions of dollars. They find niche companies, such as Biovail, whose business it is to profit by reformulating difficult molecules, or those whose only business is to develop Phase II or Phase III drugs and then license them again to a company that will market it. The Medicines Company is an example of latter business model. It is customary in the pharmaceutical industry that all data surrounding a compound is disclosed to a potential licensor under a confidentiality agreement, especially the status and results of all clinical trials.

by Barry I. Gold, Ph.D.
Cold Spring, NY, November 30, 2007

Exhibit C

UNITED STATES DISTRICT COURT

DISTRICT OF MASSACHUSETTS

JOHN HANCOCK LIFE INSURANCE COMPANY, et al Plaintiff	:	Civil Action No. 05-11150-DPW
V.	:	Courtroom No. 1
	:	1 Courthouse Way
	:	Boston, MA 02210
ABBOTT LABORATORIES, Defendant	:	2:30 p.m., Thursday October 25, 2007

Pretrial Conference

Before: THE HONORABLE DOUGLAS P. WOODLOCK,
UNITED STATES DISTRICT JUDGE

APPEARANCES:

Choate, Hall & Stewart, (by Brian A. Davis, Esq., Karen C. Troake, Esq., and Joseph H. Zwicker, Esq.) Two International Place, Boston, MA 02110, on behalf of the Plaintiffs.

Griesinger, Tighe & Maffei, LLP, (by Andrew C. Griesinger, Esq.) 176 Federal Street, Boston, MA 02110-2214, on behalf of the StoneTurn Group, LLP.

Donnelly, Conroy & Gelhaar, LLP, (by Michael S. D'Orsi, Esq.), One Beacon Street, 33rd Floor, Boston, MA 02108, on behalf of the Defendant, Abbott Laboratories.

Munger Tolles & Olson, (by Jeffrey I. Weinberger, Esq.) 335 South Grand Ave. - Suite 3500, Los Angeles, CA 90071-1560, on behalf of the Defendant, Abbott Laboratories.

Eric J. Lorenzini, Esq. 444 N. Sierra Bonita Ave., Los Angeles, CA 90036, on behalf of the Defendant, Abbott Laboratories.

that's going to be meaningful.

Mr. Tucker, if what we're talking about here is something that is -- on the piece with Mr. Friedman's role as a damage expert, if you're talking about a Daubert challenge or something like that, I'm not sure it's going to be particularly forceful for me.

These are your experts. They seem to be people -- although I haven't spoken to Mr. Tucker -- they seem to be people of substance. I would want to look at their testimony and make my own decision about it.

So, the idea of motions in limine strikes me as not a useful deployment of resources to deal with that. I think it's probably going to be -- unless there is something about Mr. Tucker that, you know, says that he's also an expert in, say, coffee makers and toasters, kind of an all-purpose expert and consequently not worth my thinking about, I suspect I'll listen to what he has to say.

So, you think about whether or not you want to make such a motion. But, it doesn't strike me on its face as being particularly helpful, particularly useful for the parties to pursue.

I'm not sure I understand precisely what additional opinions we're talking about here and you're

not sure about that either.

MR. DAVIS: No, your Honor. There's a little bit of a discontinuity here because the expert reports were due last October, when discovery was still underway, because of a variety of extensions.

THE COURT: Right.

MR. DAVIS: So, at some point in time we do want to reconcile so that experts aren't -- for example, Mr. Friedman's report was issued in October of 2006. There've been a number of depositions that have been taken since that time. He will want to have reviewed those.

THE COURT: Well, okay. Let me take it in the broader sense, which is to bring this to rest. And so, at some point, experts have to be in a position to say: This is where I now stand, having thought about it, in light of deposition discovery, and that sort of thing. That doesn't mean expanding on those opinions, but it will be final to both sides.

So, do you want a date?

MR. DAVIS: Yes.

THE COURT: What date?

MR. DAVIS: December 1.

THE COURT: Is that a reasonable date?

MR. WEINBERGER: Well, your Honor, all of the

-- the fact that depositions were done before we did expert discovery --

THE COURT: Well, I understand that.

But, what happened -- I mean, you know --

MR. DAVIS: No, they weren't.

THE COURT: The reason that your -- why this is a high-maintenance case is that money appears to be no object. In lower-maintenance cases in which money is an object, I try to tighten up more recognizing that every time a deposition is taken that an expert rethinks what they think.

I want this -- I want you to have had an opportunity to explore what the expert thinks, but, ultimately, I want an expert opinion, which is going to be in the affidavit, in the form of the affidavit, ultimately, to be the one that the expert is prepared to stand on at that point.

Now, what that means for me is that the expert doesn't all of a sudden start offering opinions on some new issue or some broader issue, but they can refine their reports so that you know what his last -- or her last and best offer is about testimony.

MR. WEINBERGER: I guess, your Honor, I don't have a problem with experts permitted to update his reports to reflect any depositions that were taken after

this. But, what I do have a problem with is all of a sudden having all kinds of new opinions that could have been made before. We have no right -- ability to take discovery.

THE COURT: I agree.

MR. DAVIS: And, I do as well.

THE COURT: Okay.

So, we'll use the December 1 date for the submission of the final expert reports which will be simply refinements and not expansions of the opinions that they rendered within the discovery period.

Now, the unreliability of Mr. Fairweather. I don't know what to say about it. But, I understand that somebody is concerned about this. But, is this the time to talk about it?

MR. WEINBERGER: Well, your Honor, I -- this is -- obviously, it's not a jury trial. This is clearly a motion we would bring in a jury situation. If the Court's preference is to, as with the damages, to wait and to hear it and then to decide and move either in the middle of the trial or the end, we have no problem with that.

We wanted to put the Court on notice that we have serious scientific problems with this opinion.

THE COURT: Well, I think that my view, I

THE COURT: All right. Thank you very much.

THE CLERK: All rise.

(Whereupon the hearing was concluded.)

CERTIFICATE

I, Marie L. Cloonan, Official Reporter of the United States District Court, do hereby certify that the foregoing transcript, from Page 1 to Page 62, constitutes to the best of my skill and ability a true and accurate transcription of my stenotype notes taken in the matter of Civil Action No. 05-11510-DPW, John Hancock Life Insurance Company, et al v. Abbott Laboratories.

Marie L. Cloonan

Official Court Reporter